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FILE COVERS 1907 - 21 Oct 2009 VOL 151 ISS 17  
 FILE LAST UPDATED: 20 Oct 2009 (20091020/ED)  
 REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009  
 USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

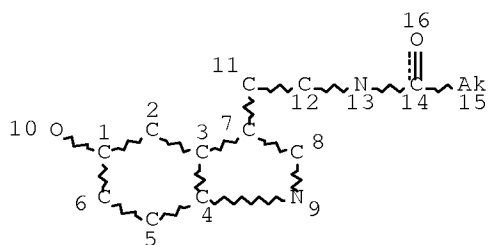
HCAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2009.

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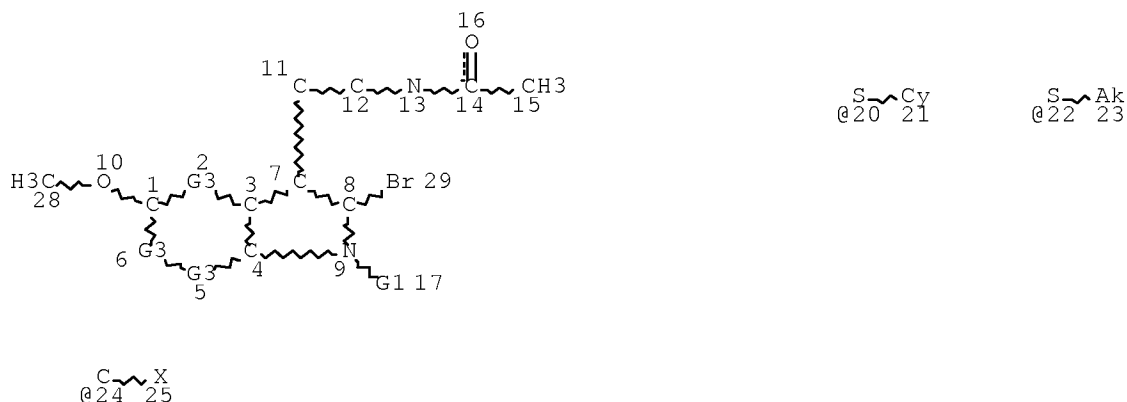
=> d stat que 138  
 L3 STR



NODE ATTRIBUTES:  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE  
 L5 2378 SEA FILE=REGISTRY SSS FUL L3  
 L15 STR



VAR G1=AK/CY/20/22

VAR G3=CH/24

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE

L16 19 SEA FILE=REGISTRY SUB=L5 SSS FUL L15

L38 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L16

=> d ibib abs hitstr 138 1-7

L38 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:1237889 HCAPLUS Full-text

DOCUMENT NUMBER: 149:417852

TITLE: Novel bromo-melatonin derivatives as potentially effective drugs to treat bone diseases

AUTHOR(S): Suzuki, Nobuo; Somei, Masanori; Seki, Azusa; Reiter, Russel J.; Hattori, Atsuhiko

CORPORATE SOURCE: Noto Marine Laboratory, Institute of Nature and Environmental Technology, Kanazawa University, Housu-gun, Ishikawa, Japan

SOURCE: Journal of Pineal Research (2008), 45(3), 229-234  
CODEN: JPRSE9; ISSN: 0742-3098

PUBLISHER: Wiley-Blackwell

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Several reports indicate that melatonin is involved in the regulation of bone metabolism. To examine the direct effect of melatonin on osteoclasts and osteoblasts, we developed an in vitro assay using fish scales that contain osteoclasts, osteoblasts, and bone matrix, all of which are similar to those found in mammalian membrane bone. Using the assay, we demonstrated that melatonin suppressed osteoclastic and osteoblastic activities. These findings are in agreement with the reports from in vivo studies in mice and rats. In an attempt to develop mols. that increase bone mass, novel bromo-melatonin derivs. were synthesized, and the effects of these

chems. on osteoclasts and osteoblasts using the scale assay were examined. As a result, novel bromo-melatonin derivs. with the ability to possibly increase bone formation were identified. In scale osteoclasts, particularly, 1-benzyl-2,4,6-tribromo-melatonin had a more potent activity than melatonin. In reference to osteoblasts, this agent (10<sup>-9</sup>-10<sup>-6</sup> M) significantly activated osteoblasts. The effect of 1-benzyl-2,4,6-tribromo-melatonin on bone formation was confirmed in ovariectomized rats. Thus, the oral administration of 1-benzyl-2,4,6-tribromo-melatonin augmented the total bone mineral d. of the femoral metaphysis of ovariectomized rats. The stress-strain index of the diaphysis in 1-benzyl-2,4,6-tribromo-melatonin-treated rats significantly increased in comparison with that in ovariectomized rats. In rats fed a low-calcium diet, the total bone mineral d. of the femoral metaphysis significantly increased following the oral administration of 1-benzyl-2,4,6-tribromo-melatonin. These studies identified a melatonin derivative that may have potential use in the treatment of bone diseases, such as osteoporosis.

IT 864546-07-6, 1-Propargyl-2,4,6-Tribromo-melatonin

864546-08-7, 1-Allyl-2,4,6-Tribromo-melatonin

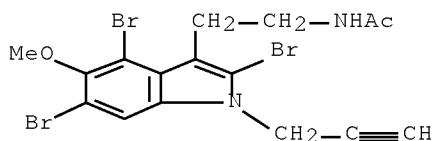
864546-09-8, 1-Benzyl-2,4,6-Tribromo-melatonin

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(novel bromo-melatonin derivs. as potentially effective drugs to treat bone diseases)

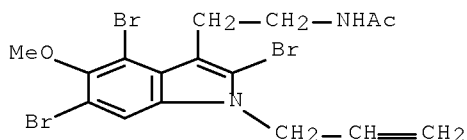
RN 864546-07-6 HCAPLUS

CN Acetamide, N-[2-[2,4,6-tribromo-5-methoxy-1-(2-propyn-1-yl)-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



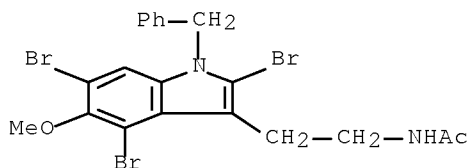
RN 864546-08-7 HCAPLUS

CN Acetamide, N-[2-[2,4,6-tribromo-5-methoxy-1-(2-propen-1-yl)-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



RN 864546-09-8 HCAPLUS

CN Acetamide, N-[2-[2,4,6-tribromo-5-methoxy-1-(phenylmethyl)-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)  
 REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:462432 HCAPLUS Full-text

DOCUMENT NUMBER: 149:45397

TITLE: Novel bromomelatonin derivatives suppress osteoclastic activity and increase osteoblastic activity: implications for the treatment of bone diseases

AUTHOR(S): Suzuki, Nobuo; Somei, Masanori; Kitamura, Kei-Ichiro; Reiter, Russel J.; Hattori, Atsuhiko

CORPORATE SOURCE: Noto Marine Laboratory, Institute of Nature and Environmental Technology, Kanazawa University, Housu-gun, Ishikawa, Japan

SOURCE: Journal of Pineal Research (2008), 44(3), 326-334  
 CODEN: JPRSE9; ISSN: 0742-3098

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The teleost scale is a calcified tissue that contains osteoclasts, osteoblasts, and bone matrix, all of which are similar to those found in mammalian membrane bone. Using the goldfish scale, we recently developed a new in vitro assay system and previously demonstrated that melatonin suppressed both osteoclastic and osteoblastic activities in this assay system. In mammals, 2-bromomelatonin possesses a higher affinity for the melatonin receptor than does melatonin. Using a newly developed synthetic method, we synthesized 2-bromomelatonin, 2,4,6-tribromomelatonin and novel bromomelatonin derivs. (1-allyl-2,4,6-tribromomelatonin, 1-propargyl-2,4,6-tribromomelatonin, 1-benzyl-2,4,6-tribromomelatonin, and 2,4,6,7-tetrabromomelatonin) and then examined the effects of these chems. on osteoclasts and osteoblasts. All bromomelatonin derivs., as well as melatonin, had an inhibitory action on osteoclasts. In particular, 1-benzyl-2,4,6-tribromomelatonin (benzyl-tribromomelatonin) possessed a stronger activity than melatonin. At an in vitro concentration of 10<sup>-10</sup> M, benzyl-tribromomelatonin still suppressed osteoclastic activity after 6 h of incubation. In reference to osteoblasts, all bromomelatonin derivs. had a stimulatory action, although melatonin inhibited osteoblastic activity. In addition, estrogen receptor mRNA expression (an osteoblastic marker) was increased in benzyl-tribromomelatonin (10<sup>-7</sup> M)-treated scales. Taken together, the present results strongly suggest that these novel melatonin derivs. have significant potential for use as beneficial drug for bone diseases such as osteoporosis.

IT 864546-07-6P, 1-Propargyl-2,4,6-tribromomelatonin

864546-08-7P, 1-Allyl-2,4,6-tribromomelatonin

864546-09-8P, 1-Benzyl-2,4,6-tribromomelatonin

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);

PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU

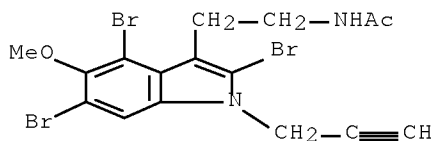
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

## (Uses)

(novel bromomelatonin derivs. suppress osteoclastic activity and increase osteoblastic activity: implications for treatment of bone diseases)

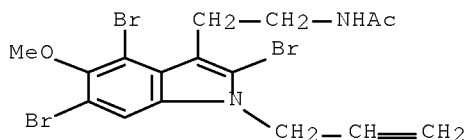
RN 864546-07-6 HCAPLUS

CN Acetamide, N-[2-[2,4,6-tribromo-5-methoxy-1-(2-propyn-1-yl)-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



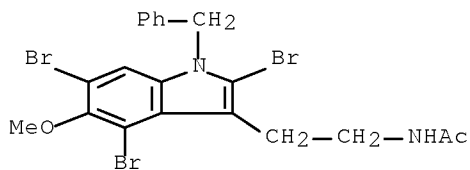
RN 864546-08-7 HCAPLUS

CN Acetamide, N-[2-[2,4,6-tribromo-5-methoxy-1-(2-propen-1-yl)-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



RN 864546-09-8 HCAPLUS

CN Acetamide, N-[2-[2,4,6-tribromo-5-methoxy-1-(phenylmethyl)-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2007:82570 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 146:163392

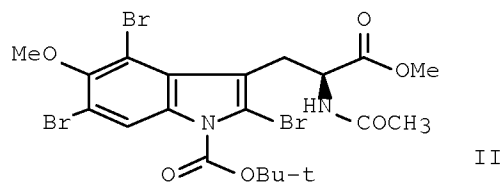
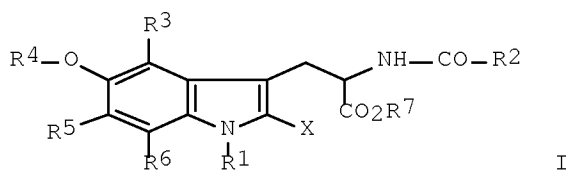
TITLE: Preparation of tryptophan derivatives for the treatment of osteoporosis

INVENTOR(S): Somei, Masanori; Hattori, Atsuhiko; Suzuki, Nobuo

PATENT ASSIGNEE(S): National University Corporation Kanazawa University, Japan; National University Corporation Tokyo Medical

SOURCE: and Dental University  
PCT Int. Appl., 28pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007010723	A1	20070125	WO 2006-JP312978	20060629
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1911744	A1	20080416	EP 2006-767595	20060629
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
US 20090054511	A1	20090226	US 2008-7992	20080117
CN 101233105	A	20080730	CN 2006-80026616	20080121
PRIORITY APPLN. INFO.:			JP 2005-209753	A 20050720
			WO 2006-JP312978	W 20060629
OTHER SOURCE(S):			MARPAT 146:163392	
GI				



AB Title compds. I [X = halo; R1 = H, (un)substituted alkyl, (un)substituted alkenyl, etc.; R2 = (un)substituted alkyl; R3, R5, R6 = H, halo; R4 = H, (un)substituted alkyl; R7 = H, (un)substituted hydrocarbon group] and salts

thereof were prepared. For example, reaction of (S)-N-acetyl-2,4,6-tribromo-5-methoxytryptophan Me ester, e.g., prepared from (S)-N-acetyl-5-methoxytryptophan Me ester, with BOC2O afforded compound II. The disclosed tryptophan derivs. were tested for the influences by tartarate resistant acid phosphatase (TRAP) and alkali phosphatase (ALP), and showed inhibition of osteoclast and activation of osteoblast.

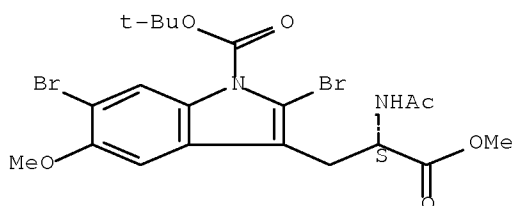
IT 920516-24-1P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of tryptophan derivs. for the treatment of osteoporosis)

RN 920516-24-1 HCAPLUS

CN L-Tryptophan, N-acetyl-2,6-dibromo-1-[(1,1-dimethylethoxy)carbonyl]-5-methoxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 920516-20-7P 920516-21-8P 920516-22-9P

920516-23-0P

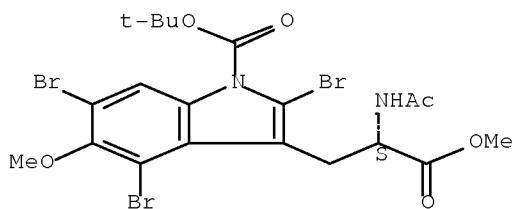
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of tryptophan derivs. for the treatment of osteoporosis)

RN 920516-20-7 HCAPLUS

CN L-Tryptophan, N-acetyl-2,4,6-tribromo-1-[(1,1-dimethylethoxy)carbonyl]-5-methoxy-, methyl ester (CA INDEX NAME)

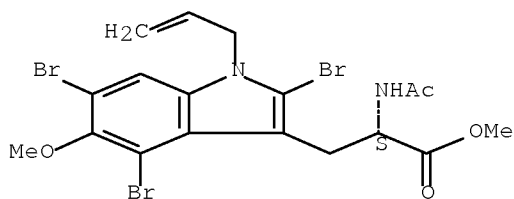
Absolute stereochemistry. Rotation (+).



RN 920516-21-8 HCAPLUS

CN L-Tryptophan, N-acetyl-2,4,6-tribromo-5-methoxy-1-(2-propen-1-yl)-, methyl ester (CA INDEX NAME)

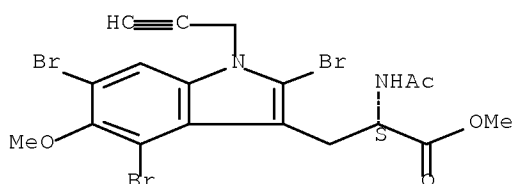
Absolute stereochemistry. Rotation (+).



RN 920516-22-9 HCAPLUS

CN L-Tryptophan, N-acetyl-2,4,6-tribromo-5-methoxy-1-(2-propyn-1-yl)-, methyl ester (CA INDEX NAME)

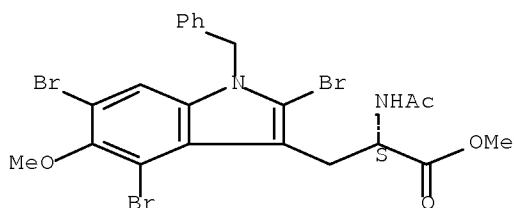
Absolute stereochemistry. Rotation (+).



RN 920516-23-0 HCAPLUS

CN L-Tryptophan, N-acetyl-2,4,6-tribromo-5-methoxy-1-(phenylmethyl)-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:319103 HCAPLUS Full-text

DOCUMENT NUMBER: 144:343589

TITLE:  $\alpha$ 2 RECEPTOR BLOCKING AGENT CONTAINING INDOLE DERIVATIVE AS ACTIVE INGREDIENT AND VASODILATOR

INVENTOR(S): Somei, Masanori; Shigenobu, Koki; Tanaka, Yoshio

PATENT ASSIGNEE(S): National University Corporation Kanazawa University, Japan; The Toho University

SOURCE: PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

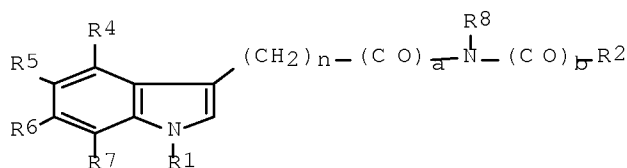
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1



## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006035617	A1	20060406	WO 2005-JP17109	20050916
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM JP 2006089443 A 20060406 JP 2004-280104 20040927 JP 3964417 B2 20070822 US 20090005430 A1 20090101 US 2007-663748 20070823 PRIORITY APPLN. INFO.: JP 2004-280104 A 20040927 WO 2005-JP17109 W 20050916 OTHER SOURCE(S): MARPAT 144:343589 GI				

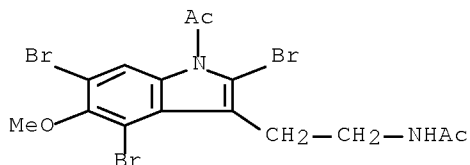


AB A compound having a simpler structure than yohimbine, which is a pentacyclic fused heterocyclic compound, and having an activity similar to that of yohimbine. Also provided is an  $\alpha_2$  receptor blocking medicine or food composition containing either a compound represented by the formula : [Chemical formula I] (wherein R1 represents hydrogen, alkyl, alkenyl, alkynyl, an aromatic group, aralkyl, acyl, arylsulfonyl, alkylsulfonyl, or hydroxy; R2 represents a hydrocarbon group; R3, R4, R5, R6, and R7 are the same or different and each represents hydrogen, halogeno, alkyl, or alkoxy; R8 represents hydrogen or acyl; n is an integer of 1-6; and a and b are the same or different and each is 1 or 0) or a pharmaceutically acceptable salt thereof.

IT 300662-22-0, 1-Acetyl-2,4,6-tribromomelatonin  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (indole and melatonin derivs. as  $\alpha_2$ -adrenergic receptor antagonists and vasodilators)

RN 300662-22-0 HCAPLUS

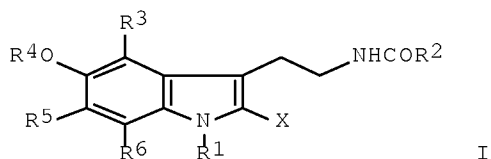
CN Acetamide, N-[2-(1-acetyl-2,4,6-tribromo-5-methoxy-1H-indol-3-yl)ethyl]- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD  
(2 CITINGS)  
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2009 ACS on STN  
ACCESSION NUMBER: 2005:1004558 HCAPLUS Full-text  
DOCUMENT NUMBER: 143:306168  
TITLE: Preparation of indole derivatives for treatment of  
osteoporosis  
INVENTOR(S): Somei, Masanori; Hattori, Atsuhiko; Suzuki, Nobuo  
PATENT ASSIGNEE(S): Kanazawa University Technology Licensing Organization  
Ltd., Japan  
SOURCE: PCT Int. Appl., 44 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005084664	A1	20050915	WO 2005-JP3743	20050304
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2005289985	A	20051020	JP 2005-61080	20050304
JP 4014052	B2	20071128		
US 20070197629	A1	20070823	US 2006-591899	20060907
PRIORITY APPLN. INFO.:			JP 2004-64408	A 20040308
			WO 2005-JP3743	W 20050304
OTHER SOURCE(S):			MARPAT 143:306168	
GI				



AB Title compds. represented by the formula I [wherein X = halo; R1 = H, (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = (un)substituted alkyl; R3, R5, R6 = independently H or halo; R4 = H or (un)substituted alkyl; and pharmaceutically acceptable salts thereof] were prepared for treatment of osteoporosis. For example, reaction of I (X = R3 = R5 = Br, R2 = R4 = Me, R1 = H) with propargyl chloride gave I (R2-R6 are defined as above, R1 = CH.tplbond.CCH2) in 97% yield. The indole derivs. were tested for the influences received by bone cell (TRAP activity) and osteoblastic cell (ALP activity), and showed inhibition of osteoclast and activation of osteoblastic cell. Thus, I and their pharmaceutical compns. are useful for the treatment of osteoporosis.

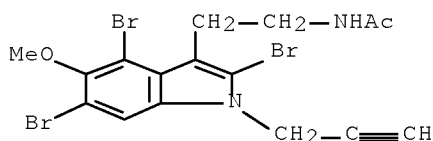
IT 864546-07-6P 864546-08-7P 864546-09-8P  
864546-10-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of indole derivs. for treatment of osteoporosis)

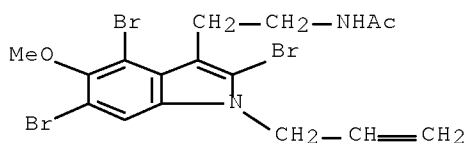
RN 864546-07-6 HCAPLUS

CN Acetamide, N-[2-[2,4,6-tribromo-5-methoxy-1-(2-propyn-1-yl)-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



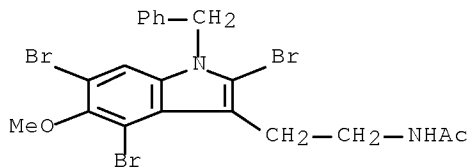
RN 864546-08-7 HCAPLUS

CN Acetamide, N-[2-[2,4,6-tribromo-5-methoxy-1-(2-propen-1-yl)-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



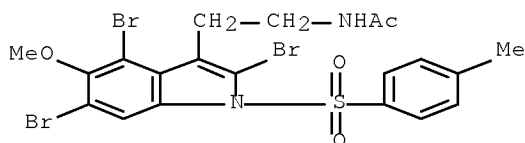
RN 864546-09-8 HCAPLUS

CN Acetamide, N-[2-[2,4,6-tribromo-5-methoxy-1-(phenylmethyl)-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



RN 864546-10-1 HCAPLUS

CN Acetamide, N-[2-[2,4,6-tribromo-5-methoxy-1-[(4-methylphenyl)sulfonyl]-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:557901 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 133:296316

TITLE: Syntheses of melatonin and its derivatives

AUTHOR(S): Somei, Masanori; Fukui, Yoshikazu; Hasegawa, Masakazu; Oshikiri, Naoki; Hayashi, Toshikatsu

CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Kanazawa University, Kanazawa, 920-0934, Japan

SOURCE: Heterocycles (2000), 53(8), 1725-1736

CODEN: HTCYAM; ISSN: 0385-5414

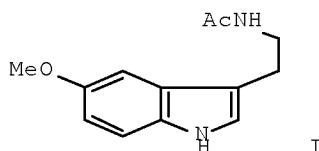
PUBLISHER: Japan Institute of Heterocyclic Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

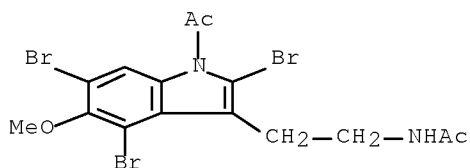
OTHER SOURCE(S): CASREACT 133:296316

GI



AB Two simple synthetic methods for melatonin (I) are newly developed from tryptamine through intermediates, which are promising lead compds. for drug developing research. Novel chemical reactivities of melatonin in its bromination, lithiation, and acylation are also reported.

IT 300662-22-0P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (synthesis of melatonin and derivs.)  
 RN 300662-22-0 HCAPLUS  
 CN Acetamide, N-[2-(1-acetyl-2,4,6-tribromo-5-methoxy-1H-indol-3-yl)ethyl]-  
 (CA INDEX NAME)



OS.CITING REF COUNT: 22 THERE ARE 22 CAPLUS RECORDS THAT CITE THIS  
 RECORD (23 CITINGS)  
 REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1995:996976 HCAPLUS Full-text

DOCUMENT NUMBER: 124:175864

ORIGINAL REFERENCE NO.: 124:32611a,32614a

TITLE: Preparation of spiro[indole-3,3'-pyrrolidine]  
 derivatives as melatoninergetic agonists

INVENTOR(S): Fourtillan, Jean-Bernard; Fourtillan, Marianne;  
 Jacquesy, Jean-Claude; Jouannetaud, Marie-Paule;  
 Violeau, Bruno; Karam, Omar

PATENT ASSIGNEE(S): CEMAF, Fr.

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

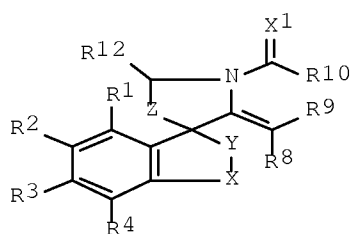
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

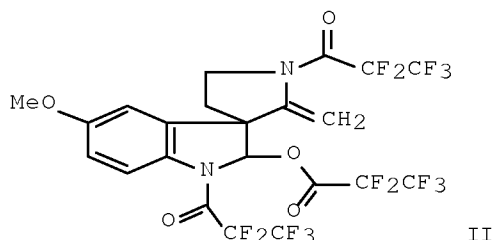
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9527712	A1	19951019	WO 1995-FR443	19950406
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2718445	A1	19951013	FR 1994-4102	19940407
FR 2718445	B1	19960628		
FR 2724170	A1	19960308	FR 1994-10558	19940902
FR 2724170	B1	19970530		
AU 9523108	A	19951030	AU 1995-23108	19950406
EP 754183	A1	19970122	EP 1995-916720	19950406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1148855	A	19970430	CN 1995-192961	19950406
CN 1047386	C	19991215		
JP 09511514	T	19971118	JP 1995-526122	19950406
ZA 9509826	A	19960529	ZA 1995-9826	19951120

# US 10/591899

US 5763471 A 19980609 US 1996-722105 19961211  
 PRIORITY APPLN. INFO.: FR 1994-4102 A 19940407  
 FR 1994-10558 A 19940902  
 WO 1995-FR443 W 19950406  
 OTHER SOURCE(S): CASREACT 124:175864; MARPAT 124:175864  
 GI



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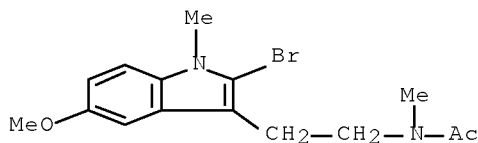


II

AB Title compds. [I; R1-R4 = H, halo, alkyl, alkoxy, etc.; R8,R9 = H, alkyl, aryl(alkyl); R10 = H, alkyl, aryl, etc.; R12 = H, alkyl; XY = NR5CR6R7, NR5C(:X3), N:CR14; R5 = H, alkyl, aryl, etc.; R6,R7 = H, alkyl, aryl, etc.; R14 = H, alkyl, alkoxy, etc.; X1,X3 = O, S, (alkyl)imino; Z = CH2, CH2CH2] were prepared Thus, melatonin was treated with pentafluoropropionic anhydride to give title compound II. Data for sedative-hypnotic activity of I in vivo were given.

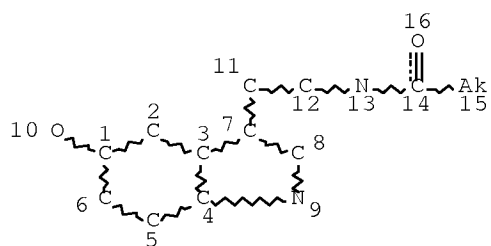
IT 173589-57-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of spiro[indole-3,3'-pyrrolidine] derivs. as melatoninerigic agonists)

RN 173589-57-6 HCAPLUS  
 CN Acetamide, N-[2-(2-bromo-5-methoxy-1-methyl-1H-indol-3-yl)ethyl]-N-methyl- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)  
 REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

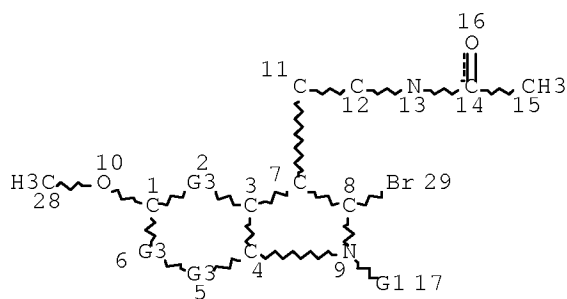
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

L5 2378 SEA FILE=REGISTRY SSS FUL L3

L15 STR



S Cy  
@20 21

S Ak  
@22 23

C X  
@24 25

VAR G1=AK/CY/20/22

VAR G3=CH/24

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

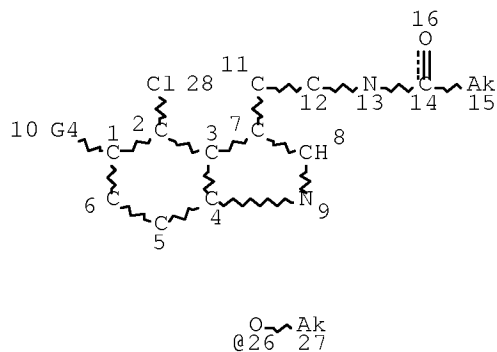
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NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE

L16 19 SEA FILE=REGISTRY SUB=L5 SSS FUL L15

L23 STR



VAR G4=OH/26

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

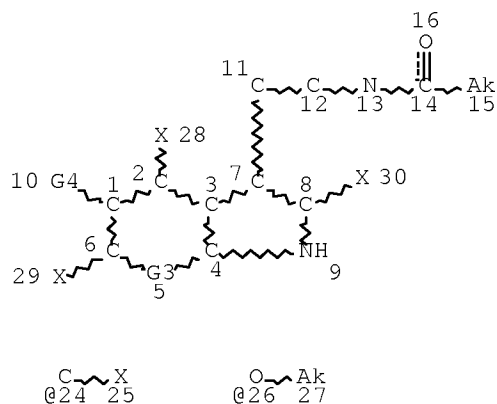
GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

L25 STR



VAR G3=CH/24

VAR G4=OH/26

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

L27 15 SEA FILE=REGISTRY SUB=L5 SSS FUL L23 OR L25

L38 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L16

L39 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L27

L40 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L39 NOT L38



=&gt; d ibib abs hitstr 140 1-3

L40 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1993:254747 HCAPLUS Full-text

DOCUMENT NUMBER: 118:254747

ORIGINAL REFERENCE NO.: 118:44261a,44264a

TITLE: Tryptamine analogues, their synthesis and their use as 5-HT1-like or 5-HT2 receptor agonists

INVENTOR(S): Kruse, Lawrence Ivan; Young, Rodney Christopher; Kaumann, Alberto Julio

PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

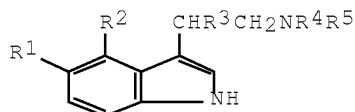
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

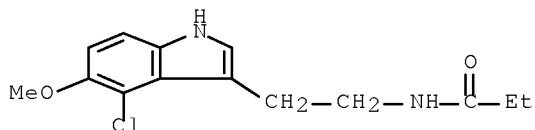
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9300333	A1	19930107	WO 1992-GB1089	19920617
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
AU 9219288	A	19930125	AU 1992-19288	19920617
EP 593513	A1	19940427	EP 1992-912269	19920617
EP 593513	B1	19981028		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 06508354	T	19940922	JP 1992-511317	19920617
AT 172723	T	19981115	AT 1992-912269	19920617
ZA 9204523	A	19931220	ZA 1992-4523	19920619
CA 2110574	A1	19930107	CA 1992-2110574	19920717
US 5571833	A	19961105	US 1994-167890	19940526
PRIORITY APPLN. INFO.:			GB 1991-13382	A 19910621
			GB 1991-13385	A 19910621
			WO 1992-GB1089	A 19920617
OTHER SOURCE(S):		MARPAT 118:254747		
GI				



I

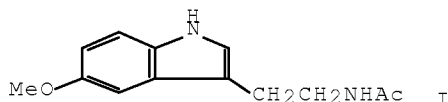
AB Title compds. I (R1 = H, HO, C1-4 alkoxy, halo-C1-4-alkoxy, C3-7-cycloalkyl-C1-4-alkoxy, aryloxy, aryl-C1-4-alkoxy; R2 = halo, C1-4 alkyl, NC, O2N, F3C; R3 = H, C1-4 alkyl; R4, R5 = H, C1-4 alkyl, R4R5N = ring), were prepared Thus, 3-(cyanomethyl)-4-chloro-5-(benzyloxy)indole (preparation given) in MeOH/NH3 was hydrogenated over Raney Ni to give I (R1 = PhCH2O, R2 = Cl, R3 = H, R4 = R5 Me) which was hydrogenated over Pd-C and treated with (CO2H)2 to give I (R1 = HO, R2 = Cl, R3 = H, R4 = R5 = Me) oxalate (II). In test for 5-HT1-like and 5-HT2 receptor screens, the EC50 of II was 0.2-15 and 0.2  $\mu$ M, resp. Pharmaceutical formulations containing I are given.

IT 147405-70-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reaction of, in preparation of serotonergic agonists)  
 RN 147405-70-7 HCAPLUS  
 CN Propanamide, N-[2-(4-chloro-5-methoxy-1H-indol-3-yl)ethyl]- (CA INDEX  
 NAME)



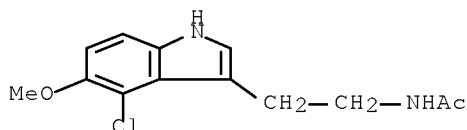
OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS  
 RECORD (13 CITINGS)  
 REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 1981:41707 HCAPLUS [Full-text](#)  
 DOCUMENT NUMBER: 94:41707  
 ORIGINAL REFERENCE NO.: 94:6713a,6716a  
 TITLE: Structure-activity relationship of melatonin analogs  
 AUTHOR(S): Frohn, M. A.; Seaborn, C. J.; Johnson, D. W.;  
 Phillipou, G.; Seamark, R. F.; Matthews, C. D.  
 CORPORATE SOURCE: Dep. Obstet. Gynaecol., Queen Elizabeth Hosp.,  
 Woodville, 5011, Australia  
 SOURCE: Life Sciences (1980), 27(22), 2043-6  
 CODEN: LIFSAK; ISSN: 0024-3205  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



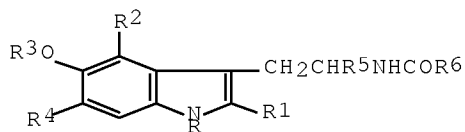
AB Anal. of the structure-activity relation between 23 indoleamines and melatonin  
 (I) [73-31-4] based on a specific in vivo fish bioassay, is described. The  
 results clearly define that only halogenation at position 6 or extension of  
 the acetyl side-chain to propionyl or butyryl is tolerated without a decrease  
 in activity. Removal of the indole double bond however, only leads to <10-  
 fold loss of activity. The over-all relevance of the data in the development  
 of a metabolically stable I agonist is discussed.  
 IT 68935-44-4  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); PRP (Properties); BIOL (Biological study)  
 (biol. activity of, structure in relation to)  
 RN 68935-44-4 HCAPLUS

CN Acetamide, N-[2-(4-chloro-5-methoxy-1H-indol-3-yl)ethyl]- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD  
(4 CITINGS)

L40 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 1979:48848 HCAPLUS Full-text  
 DOCUMENT NUMBER: 90:48848  
 ORIGINAL REFERENCE NO.: 90:7741a,7744a  
 TITLE: Synthesis and evaluation of the antioviulatory activity  
 of a variety of melatonin analogs  
 AUTHOR(S): Flaugh, Michael E.; Crowell, Thomas A.; Clemens, James  
 A.; Sawyer, Barry D.  
 CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN,  
 USA  
 SOURCE: Journal of Medicinal Chemistry (1979), 22(1), 63-9  
 CODEN: JMCMAR; ISSN: 0022-2623  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



I

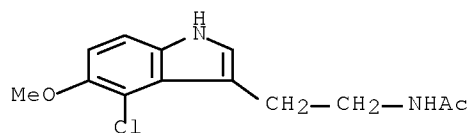
AB The synthesis and ovulation-inhibiting activity in rats of 14 melatonin [73-31-4] analogs I (R and R1 = H or Me; R2 = H or Cl; R3 = H, Me, Et, or Pr; R4 = H, Me, Cl, or F; R5 = H or Me; R6 = Me, Et, Pr, or adamantyl) is described. The halogenated derivs. I (R = R1 = R2 = R5 = H, R3 = R6 = Me, R4 = Cl) [63762-74-3] and I (R = R1 = R2 = R5 = H, R3 = R6 = Me, R4 = F) [62106-00-7] displayed a pronounced enhancement of ovulation-inhibiting activity. Structure-activity relations are discussed.

IT ~~68935-44-4P~~

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and ovulation inhibiting activity of)

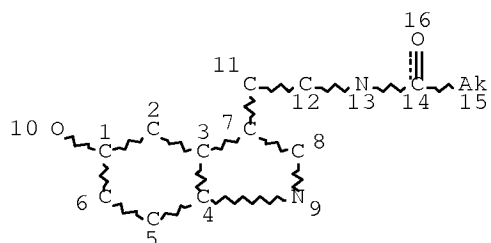
RN 68935-44-4 HCAPLUS

CN Acetamide, N-[2-(4-chloro-5-methoxy-1H-indol-3-yl)ethyl]- (CA INDEX NAME)



OS.CITING REF COUNT: 21 THERE ARE 21 CAPLUS RECORDS THAT CITE THIS  
RECORD (21 CITINGS)

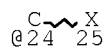
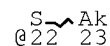
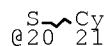
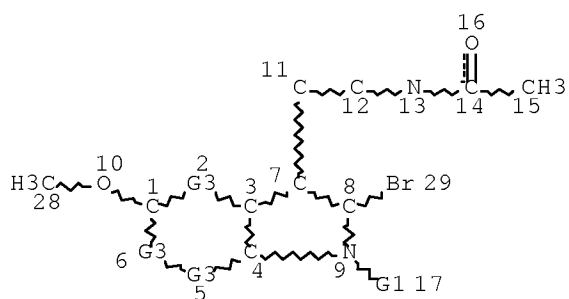
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L3 STR



NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE  
L5 2378 SEA FILE=REGISTRY SSS FUL L3  
L15 STR



VAR G1=AK/CY/20/22  
VAR G3=CH/24  
NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

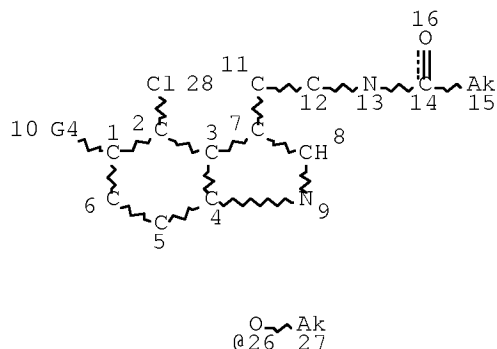
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE

L16 19 SEA FILE=REGISTRY SUB=L5 SSS FUL L15

L23 STR



VAR G4=OH/26

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

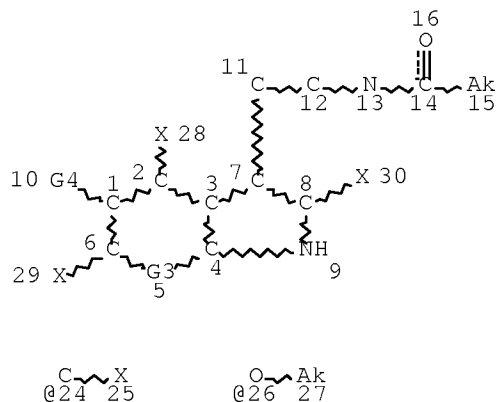
GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

L25 STR



VAR G3=CH/24

VAR G4=OH/26

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

## GRAPH ATTRIBUTES:

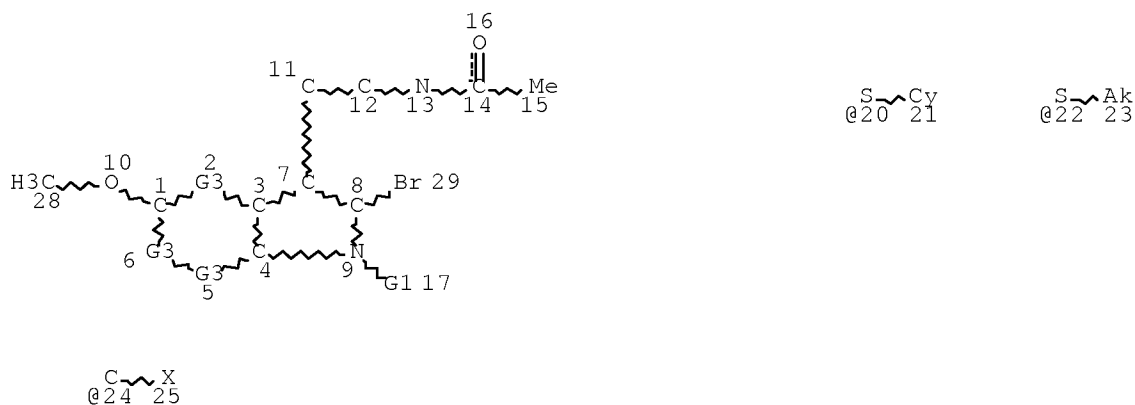
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 23

## STEREO ATTRIBUTES: NONE

L27 15 SEA FILE=REGISTRY SUB=L5 SSS FUL L23 OR L25

L28 STR



VAR G1=AK/CY/20/22

VAR G3=CH/24

## NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

## GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 25

## STEREO ATTRIBUTES: NONE

L29 19 SEA FILE=REGISTRY SUB=L5 SSS FUL L28

L38 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L16

L39 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L27

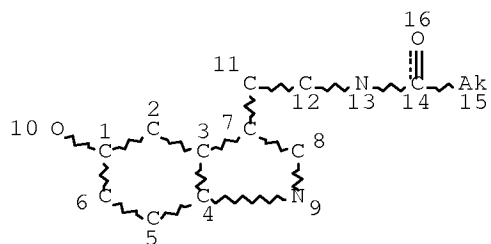
L40 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L39 NOT L38

L41 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L29

L42 0 SEA FILE=HCAPLUS ABB=ON PLU=ON L41 NOT (L38 OR L40)

=&gt; =&gt; d stat que l44

L3 STR



## NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

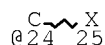
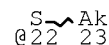
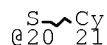
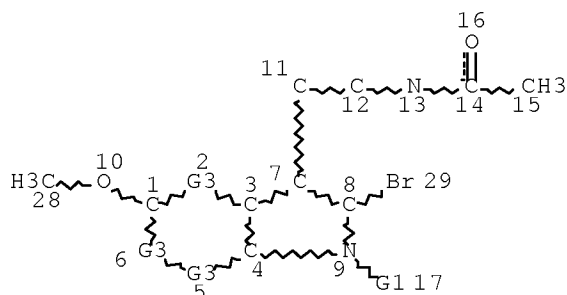
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

L5 2378 SEA FILE=REGISTRY SSS FUL L3

L15 STR



VAR G1=AK/CY/20/22

VAR G3=CH/24

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

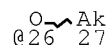
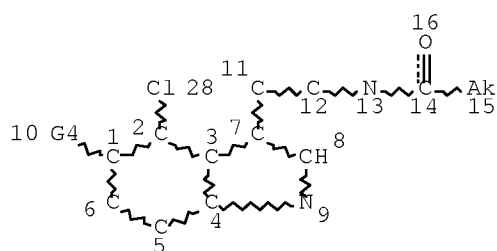
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE

L16 19 SEA FILE=REGISTRY SUB=L5 SSS FUL L15

L23 STR



VAR G4=OH/26

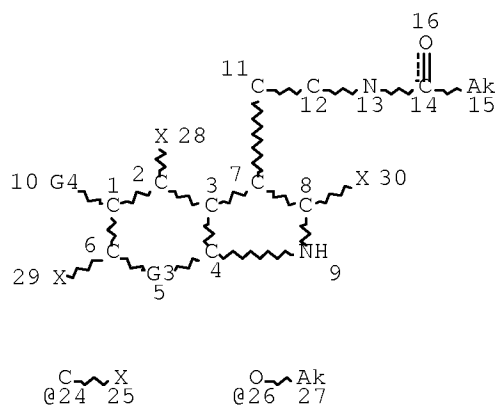
NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 19

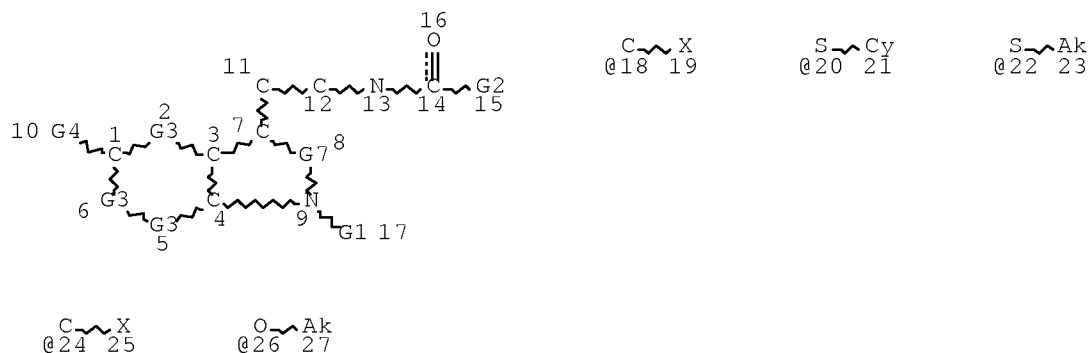
STEREO ATTRIBUTES: NONE  
L25 STR



VAR G3=CH/24  
VAR G4=OH/26  
NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE  
L27 15 SEA FILE=REGISTRY SUB=L5 SSS FUL L23 OR L25  
L34 STR



VAR G1=AK/CY/20/22/OH  
VAR G2=AK/CY  
VAR G3=CH/24  
VAR G4=OH/26  
VAR G7=CH/18  
NODE ATTRIBUTES:



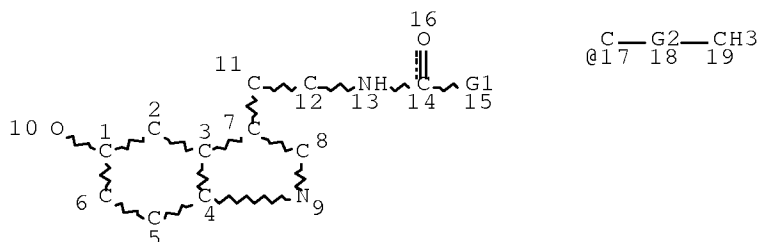
DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 27

STEREO ATTRIBUTES: NONE

L35 243 SEA FILE=REGISTRY SUB=L5 SSS FUL L34

L36 STR



VAR G1=ET/I-PR/N-PR/I-BU/S-BU/T-BU/N-BU/17/CB

REP G2=(3-19) C

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

L37 38 SEA FILE=REGISTRY SUB=L35 SSS FUL L36

L38 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L16

L39 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L27

L40 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L39 NOT L38

L43 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L37

L44 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L43 NOT (L38 OR L40)

=> d ibib abs hitstr l44 1-9

L44 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:505155 HCAPLUS Full-text

DOCUMENT NUMBER: 148:495788

TITLE: Preparation of indole derivatives, especially  
 N-[ $\beta$ -substituted  
 (5-heterocyclylalkyloxy-1H-indol-3-yl)ethyl]amides, as  
 melatonin receptors ligands and their pharmaceutical  
 compositions

INVENTOR(S): Marchand, Pascal; Babonneau, Vincent; Piessard,  
 Sylvie; Duflos, Sylvie; Boutin, Jean Albert; Audinot,  
 Valerie; Delagrangre, Philippe; Caignard, Daniel Henri

PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.

SOURCE: Fr. Demande, 22 pp.

CODEN: FRXXBL

DOCUMENT TYPE: Patent

LANGUAGE: French

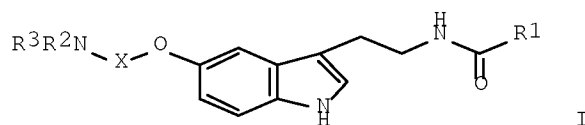
FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

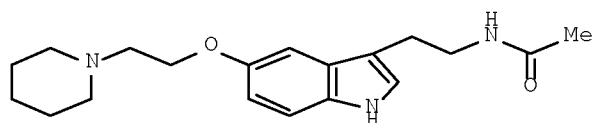
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2907451	A1	20080425	FR 2006-9113	20061018
FR 2907451	B1	20081212		
AU 2007310770	A1	20080502	AU 2007-310770	20071017
CA 2666522	A1	20080502	CA 2007-2666522	20071017
WO 2008049997	A2	20080502	WO 2007-FR1708	20071017
WO 2008049997	A3	20080912		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
EP 2079689	A2	20090722	EP 2007-858468	20071017
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
KR 2009084874	A	20090805	KR 2009-710133	20071017
CN 101522616	A	20090902	CN 2007-80037231	20090403
MX 2009004006	A	20090428	MX 2009-4006	20090416
NO 2009001779	A	20090506	NO 2009-1779	20090506
PRIORITY APPLN. INFO.:			FR 2006-9113	A 20061018
			WO 2007-FR1708	W 20071017

OTHER SOURCE(S): CASREACT 148:495788; MARPAT 148:495788

GI



I



II

AB Title compds. I [R1 = linear or branched alkyl, cycloalkyl, cycloalkylalkyl; NR2R3 = 5-8 membered heterocycle ring; X = (CH2)n; n = 2-6; and their enantiomers and diastereomers, and their and pharmaceutically acceptable acid or base addition salts] were prepared as melatonin receptors ligands. Five biol. tests are given. Thus, condensation of nitromethane with 5-methoxy-1H-indole-3-carboxaldehyde, reduction of 5-methoxy-3-(2-nitroethenyl)-1H-indole, acylation of the amine with acetic anhydride, treatment with p-tosyl chloride, demethylation of N-[2-[5-methoxy-1-[(4-methylphenyl)sulfonyl]-1H-indol-3-

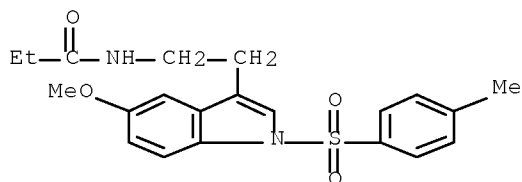
yl]ethyl]acetamide, O-alkylation of hydroxyindole with 1-(2-chloroethyl)piperidine hydrochloride, and removal of the tosyl group gave indole II. I displayed  $K_i$  values of  $< 1 \mu\text{M}$  for the binding to MT1 and MT2 melatonin receptors in an assay using 2-[125I]-iodomelatonin as radioligand. I acted powerfully on the circadian rhythm via melatoninergetic system (no data). I are useful for treating melatoninergetic system related diseases.

IT 1020701-57-8P, N-[2-[5-Methoxy-1-[(4-methylphenyl)sulfonyl]-1H-indol-3-yl]ethyl]propanamide 1020701-58-9P, N-[2-[5-Hydroxy-1-[(4-methylphenyl)sulfonyl]-1H-indol-3-yl]ethyl]propanamide 1020701-59-0P, N-[2-[1-[(4-Methylphenyl)sulfonyl]-5-[2-(1-piperidinyl)ethoxy]-1H-indol-3-yl]ethyl]propanamide 1020701-60-3P, N-[2-[5-Methoxy-1-[(4-methylphenyl)sulfonyl]-1H-indol-3-yl]ethyl]butanamide 1020701-61-4P, N-[2-[5-Hydroxy-1-[(4-methylphenyl)sulfonyl]-1H-indol-3-yl]ethyl]butanamide 1020701-62-5P, N-[2-[1-[(4-Methylphenyl)sulfonyl]-5-[2-(1-piperidinyl)ethoxy]-1H-indol-3-yl]ethyl]butanamide 1020701-63-6P  
RL: PRPH (Prophetic); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of N-[ $\beta$ -substituted  
(5-heterocyclylalkyloxy-1H-indol-3-yl)ethyl]amides as melatonin  
receptor ligands)

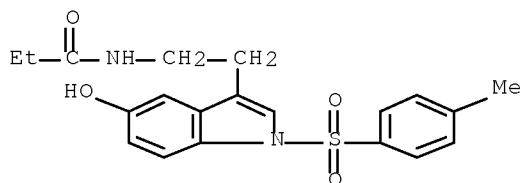
RN 1020701-57-8 HCAPLUS

CN Propanamide, N-[2-[5-methoxy-1-[(4-methylphenyl)sulfonyl]-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



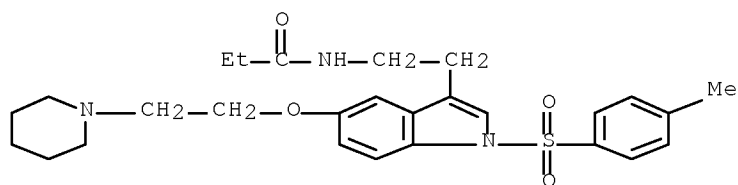
RN 1020701-58-9 HCAPLUS

CN Propanamide, N-[2-[5-hydroxy-1-[(4-methylphenyl)sulfonyl]-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



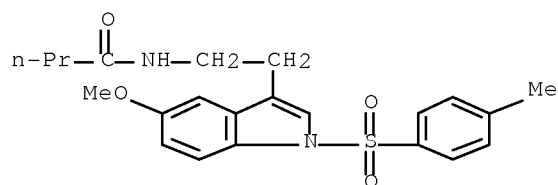
RN 1020701-59-0 HCAPLUS

CN Propanamide, N-[2-[1-[(4-methylphenyl)sulfonyl]-5-[2-(1-piperidinyl)ethoxy]-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



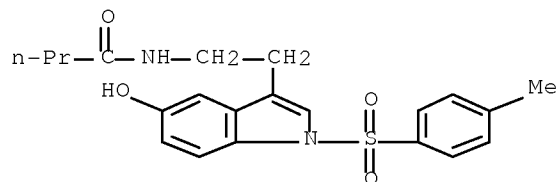
RN 1020701-60-3 HCAPLUS

CN Butanamide, N-[2-[5-methoxy-1-[(4-methylphenyl)sulfonyl]-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



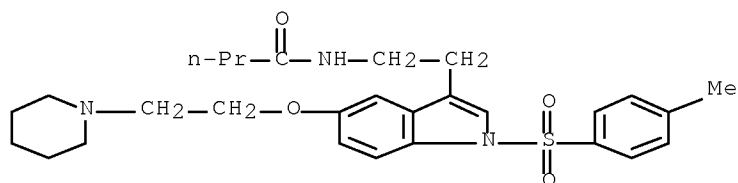
RN 1020701-61-4 HCAPLUS

CN Butanamide, N-[2-[5-hydroxy-1-[(4-methylphenyl)sulfonyl]-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



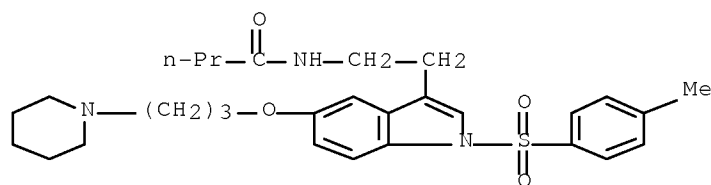
RN 1020701-62-5 HCAPLUS

CN Butanamide, N-[2-[1-[(4-methylphenyl)sulfonyl]-5-[2-(1-piperidinyl)ethoxy]-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



RN 1020701-63-6 HCAPLUS

CN Butanamide, N-[2-[1-[(4-methylphenyl)sulfonyl]-5-[3-(1-piperidinyl)propoxy]-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2007:590020 HCAPLUS Full-text

DOCUMENT NUMBER: 147:181675

TITLE: 7-Substituted-melatonin and  
7-substituted-1-methylmelatonin analogues: Effect of  
substituents on potency and binding affinity

AUTHOR(S): Faust, Ruediger; Garratt, Peter J.; Trujillo Perez,  
Maria Angeles; Piccio, Vincent J.-D.; Madsen,  
Christian; Stenstrom, Ane; Frolund, Bente; Davidson,  
Kathryn; Teh, Muy-Teck; Sugden, David

CORPORATE SOURCE: Department of Chemistry, University College London,  
London, WC1H 0AJ, UK

SOURCE: Bioorganic & Medicinal Chemistry (2007), 15(13),  
4543-4551

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 147:181675

AB A series of 7-substituted melatonin and 1-methylmelatonin analogs were prepared and tested against human and amphibian melatonin receptors. 7-Substituents reduced the agonist potency of all the analogs in the *Xenopus laevis* melanophore assay, 7-bromomelatonin (5d) and N-Butanoyl 7-bromo-5-methoxytryptamine (5f) being the most active compds., but both were 42-fold less potent than melatonin (1). Whereas all the analogs bind with lower affinity at the human MT1 receptor than melatonin, 5d, 5f and N-Propanoyl 7-bromo-5-methoxytryptamine (5e) show a similar binding affinity to melatonin at the MT2 receptor and consequently show some MT2 selectivity. These results suggest that the receptor pocket around C-7 favors binding by an electroneg. group, suggesting an electropos. region in this area of the receptor.

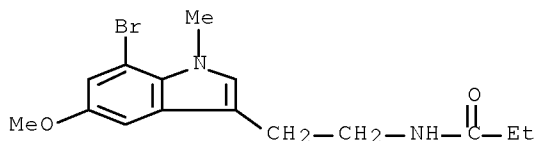
IT 944478-06-2P 944478-07-3P

RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

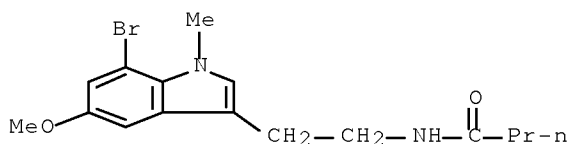
(effects of 7-Substituted-melatonin and 7-substituted-1-methylmelatonin analogs on potency and binding affinity)

RN 944478-06-2 HCAPLUS

CN Propanamide, N-[2-(7-bromo-5-methoxy-1-methyl-1H-indol-3-yl)ethyl]- (CA INDEX NAME)



RN 944478-07-3 HCAPLUS  
 CN Butanamide, N-[2-(7-bromo-5-methoxy-1-methyl-1H-indol-3-yl)ethyl]- (CA  
 INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD  
 (4 CITINGS)  
 REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:429473 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 145:116689

TITLE: Mapping the Melatonin Receptor. 7. Subtype Selective  
 Ligands Based on  $\beta$ -Substituted  
 N-Acyl-5-methoxytryptamines and  $\beta$ -Substituted  
 N-Acyl-5-methoxy-1-methyltryptamines

AUTHOR(S): Tsotinis, Andrew; Vlachou, Margarita; Papahatjis,  
 Demetris P.; Calogeropoulou, Theodora; Nikas, Spyros  
 P.; Garratt, Peter J.; Piccio, Vincent; Vonhoff,  
 Stefan; Davidson, Kathryn; Teh, Muy-Teck; Sugden,  
 David

CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Faculty of  
 Pharmacy, University of Athens, Athens, 157 71, Greece

SOURCE: Journal of Medicinal Chemistry (2006), 49(12),  
 3509-3519

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 145:116689

AB A series of  $\beta$ -substituted and  $\beta,\beta$ -disubstituted N-acyl 5-methoxy-1-methyltryptamines and 5-methoxytryptamines have been prepared as melatonin analogs to investigate the nature of the binding site of the melatonin receptor. The affinity of analogs was determined in a radioligand binding assay using cloned human MT1 and MT2 receptor subtypes expressed in NIH 3T3 cells. Agonist and antagonist potency of all analogs was measured using the pigment aggregation response of a clonal line of *Xenopus laevis* melanophores.  $\beta$ -Methylmelatonin (17a) and  $\beta,\beta$ -dimethylmelatonin (17b), though showing a slight decrease in binding at human receptors, show an increase in potency on *Xenopus*. N-Butanoyl 5-methoxy-1-methyl- $\beta,\beta$ -trimethylenetryptamine (12c) is an

antagonist at human MT1 receptors but an agonist at MT2, while N-butanoyl 5-methoxy-1-methyl- $\beta,\beta$ -tetramethylenetryptamine (13c) is an antagonist at MT1 but had no action at MT2 and is one of the first examples of an MT1 selective antagonist.

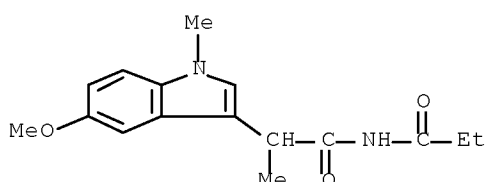
IT 896101-55-6P 896101-56-7P 896101-58-9P  
896101-59-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Mapping the Melatonin Receptor. 7. Subtype Selective Ligands Based on  $\beta$ -Substituted N-Acyl-5-methoxytryptamines and  $\beta$ -Substituted)

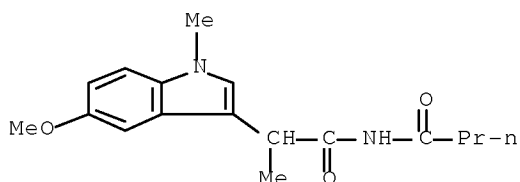
RN 896101-55-6 HCAPLUS

CN 1H-Indole-3-acetamide, 5-methoxy- $\alpha,1$ -dimethyl-N-(1-oxopropyl)- (CA INDEX NAME)



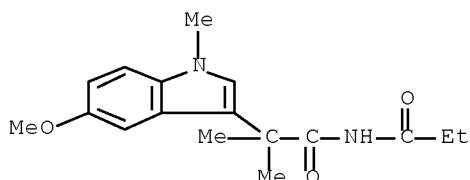
RN 896101-56-7 HCAPLUS

CN 1H-Indole-3-acetamide, 5-methoxy- $\alpha,1$ -dimethyl-N-(1-oxobutyl)- (CA INDEX NAME)



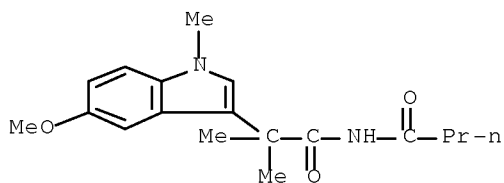
RN 896101-58-9 HCAPLUS

CN 1H-Indole-3-acetamide, 5-methoxy- $\alpha,\alpha,1$ -trimethyl-N-(1-oxopropyl)- (CA INDEX NAME)



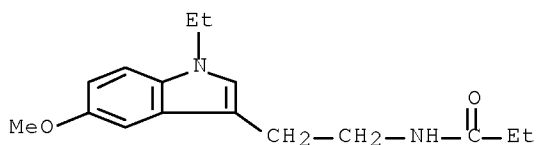
RN 896101-59-0 HCAPLUS

CN 1H-Indole-3-acetamide, 5-methoxy- $\alpha,\alpha,1$ -trimethyl-N-(1-oxobutyl)- (CA INDEX NAME)



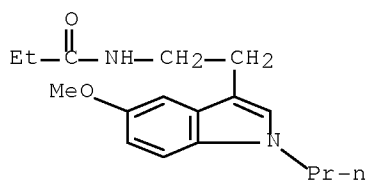
OS.CITING REF COUNT: 19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)  
 REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 2006:347137 HCAPLUS Full-text  
 DOCUMENT NUMBER: 144:460948  
 TITLE: Structure-activity relationships of antioxidant activity of some melatonin derivatives  
 AUTHOR(S): Ates Alagoz, Zeynep  
 CORPORATE SOURCE: Eczacilik Fakultesi, Farmasotik Kimya Anabilim Dalı, Ankara Universitesi, Tandogan - Ankara, 06100, Turk.  
 SOURCE: Ankara Universitesi Eczacilik Fakultesi Dergisi (2005), 34(2), 73-93  
 CODEN: AUDE5; ISSN: 1015-3918  
 PUBLISHER: Ankara Universitesi Eczacilik Fakultesi  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Turkish  
 AB In the present study, thermodyn., hydrophobic and steric parameters of melatonin and 23 derivs. were calculated to explain their physicochem. properties, and these parameters were compared with their antioxidant activity. Statistics methods, mainly regression anal., were used in the structure-activity relationship studies.  
 IT 867364-62-3 867364-63-4 867364-64-5  
 867364-65-6 867364-66-7  
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (antioxidant activity and physiochem. properties in relation to structures of melatonin derivs.)  
 RN 867364-62-3 HCAPLUS  
 CN Propanamide, N-[2-(1-ethyl-5-methoxy-1H-indol-3-yl)ethyl]- (CA INDEX NAME)



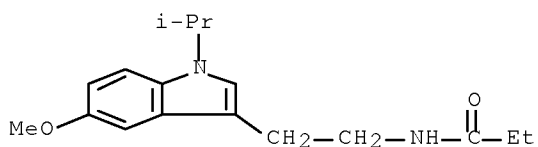
RN 867364-63-4 HCAPLUS  
 CN Propanamide, N-[2-(5-methoxy-1-propyl-1H-indol-3-yl)ethyl]- (CA INDEX NAME)





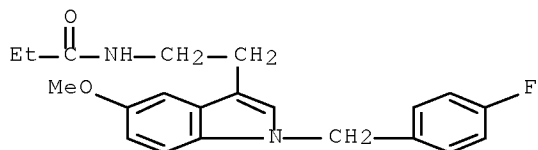
RN 867364-64-5 HCAPLUS

CN Propanamide, N-[2-[5-methoxy-1-(1-methylethyl)-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



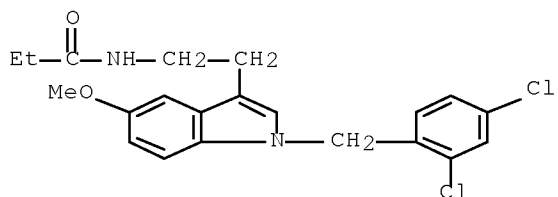
RN 867364-65-6 HCAPLUS

CN Propanamide, N-[2-[1-[(4-fluorophenyl)methyl]-5-methoxy-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



RN 867364-66-7 HCAPLUS

CN Propanamide, N-[2-[1-[(2,4-dichlorophenyl)methyl]-5-methoxy-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



L44 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 2005:1024520 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 143:399969

TITLE: Synthesis and antioxidant properties of some indole ethylamine derivatives as melatonin analogs

AUTHOR(S): Ates-Alagoz, Z.; Buyukbingol, Z.; Buyukbingol, E.  
 CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Department of Biochemistry2, Faculty of Pharmacy (ECZACILIK), University of Ankara, Tandogan, Ankara, 06100, Turk.  
 SOURCE: Pharmazie (2005), 60(9), 643-647  
 CODEN: PHARAT; ISSN: 0031-7144  
 PUBLISHER: Govi-Verlag Pharmazeutischer Verlag GmbH  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 143:399969

AB The synthesis and lipid peroxidn. (LP) inhibition activity of several novel indole melatonin analogs are reported. Compds. have shown variable antioxidant features depending on the substitution pattern. Melatonin and the antioxidant reference compound Bu hydroxy toluen (BHT) were used to compare the antioxidant capability of the compds. synthesized.

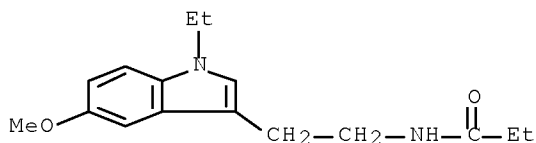
IT 867364-62-3P 867364-63-4P 867364-64-5P  
 867364-65-6P 867364-66-7P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis and antioxidant properties of some indole ethylamine derivs. as melatonin analogs)

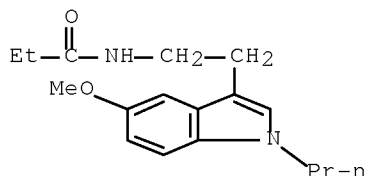
RN 867364-62-3 HCAPLUS

CN Propanamide, N-[2-(1-ethyl-5-methoxy-1H-indol-3-yl)ethyl]- (CA INDEX NAME)



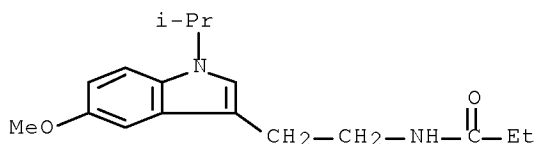
RN 867364-63-4 HCAPLUS

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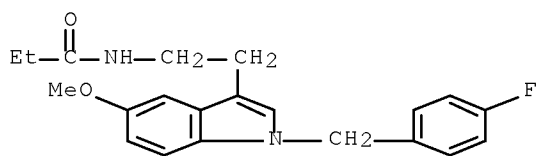
RN 867364-64-5 HCAPLUS

CN Propanamide, N-[2-[5-methoxy-1-(1-methylethyl)-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



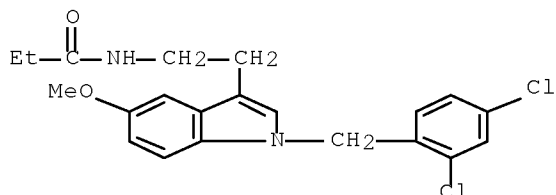
RN 867364-65-6 HCAPLUS

CN Propanamide, N-[2-[1-[(4-fluorophenyl)methyl]-5-methoxy-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



RN 867364-66-7 HCAPLUS

CN Propanamide, N-[2-[1-[(2,4-dichlorophenyl)methyl]-5-methoxy-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:19773 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 136:334735

TITLE: Synthesis of N1-phenethyl substituted indole derivatives as new melatoninerbic agonists and antagonists

AUTHOR(S): Tsotinis, Andrew; Vlachou, Margarita; Eleutheriades, Andreas; Prinea, Effie; Ebreo, Darren; The, Muy-Teck; Sugden, David

CORPORATE SOURCE: School of Pharmacy, Department of Pharmaceutical Chemistry, University of Athens, Athens, 157 71, Greece

SOURCE: Chemical &amp; Pharmaceutical Bulletin (2002), 50(1), 31-39

CODEN: CPBTAL; ISSN: 0009-2363

PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 136:334735

AB The potency of new indolic N1-phenethyl substituted melatoninergic ligands with and without Me groups in the  $\alpha$  and  $\beta$  position of the alkanamidoethyl side chain was examined using the pigment aggregation response in a clonal line of *Xenopus laevis* melanophores. The non 5-OMe substituted compds. are all weak antagonists while introduction of the 5-OMe group increases both agonist and antagonist activity except in all but one case. Introduction of an  $\alpha$ -Me group into the 5-OMe derivs. reduces the agonist potency while introduction of a  $\beta$ -Me group has only a small effect on either the agonist or antagonist potency. Double  $\beta$ -Me substitution of the 5-OMe derivs. generally increases the agonist potential and decreases the antagonist potency with one exception.

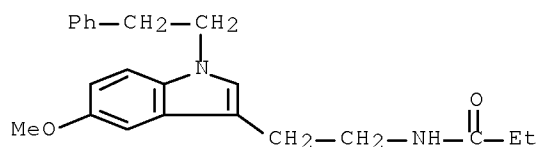
IT 416861-02-4P 416861-03-5P 416861-07-9P  
 416861-08-0P 416861-12-6P 416861-13-7P  
 416861-17-1P 416861-18-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis of phenethyl substituted indole derivs. as melatoninergic agonists and antagonists)

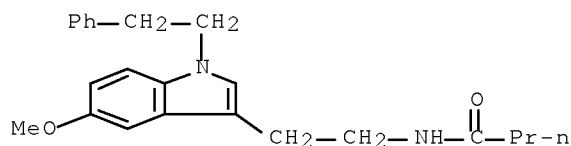
RN 416861-02-4 HCAPLUS

CN Propanamide, N-[2-[5-methoxy-1-(2-phenylethyl)-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



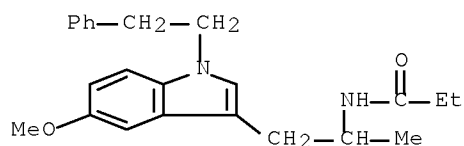
RN 416861-03-5 HCAPLUS

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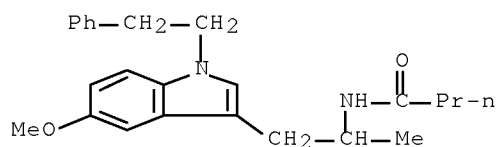
RN 416861-07-9 HCAPLUS

CN Propanamide, N-[2-[5-methoxy-1-(2-phenylethyl)-1H-indol-3-yl]-1-methylethyl]- (CA INDEX NAME)



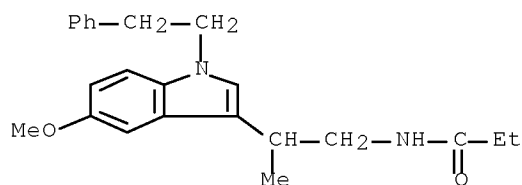
RN 416861-08-0 HCAPLUS

CN Butanamide, N-[2-[5-methoxy-1-(2-phenylethyl)-1H-indol-3-yl]-1-methylethyl]- (CA INDEX NAME)



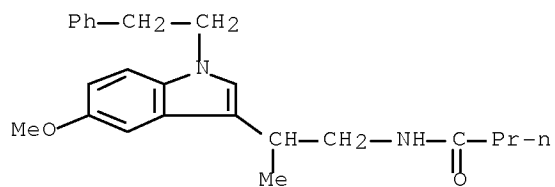
RN 416861-12-6 HCAPLUS

CN Propanamide, N-[2-[5-methoxy-1-(2-phenylethyl)-1H-indol-3-yl]propyl]- (CA INDEX NAME)



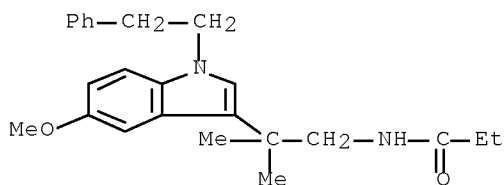
RN 416861-13-7 HCAPLUS

CN Butanamide, N-[2-[5-methoxy-1-(2-phenylethyl)-1H-indol-3-yl]propyl]- (CA INDEX NAME)

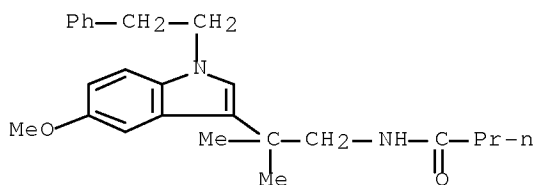


RN 416861-17-1 HCAPLUS

CN Propanamide, N-[2-[5-methoxy-1-(2-phenylethyl)-1H-indol-3-yl]-2-methylpropyl]- (CA INDEX NAME)



RN 416861-18-2 HCAPLUS  
 CN Butanamide, N-[2-[5-methoxy-1-(2-phenylethyl)-1H-indol-3-yl]-2-methylpropyl]- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)  
 REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:185117 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 132:273842

TITLE: Mapping the Melatonin Receptor. 6. Melatonin Agonists and Antagonists Derived from

6H-Isoindolo[2,1-a]indoles, 5,6-Dihydroindolo[2,1-a]isoquinolines, and 6,7-Dihydro-5H-benzo[c]azepino[2,1-a]indoles

AUTHOR(S): Faust, Ruediger; Garratt, Peter J.; Jones, Rob; Yeh, Li-Kuan; Tsotinis, Andrew; Panoussopoulou, Maria; Calogeropoulou, Theodora; Teh, Muy-Teck; Sugden, David  
 CORPORATE SOURCE: Department of Chemistry, University College London, London, WC1H 0AJ, UK

SOURCE: Journal of Medicinal Chemistry (2000), 43(6), 1050-1061

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 6H-Isoindolo[2,1-a]indoles, 5,6-dihydroindolo[2,1-a]isoquinolines, and 6,7-dihydro-5H-benzo[c]azepino[2,1-a]indoles have been prepared as melatonin analogs to investigate the nature of the binding site of the melatonin receptor. The affinity of analogs was determined in a radioligand binding assay using cloned human mtl and MT2 receptor subtypes expressed in NIH 3T3 cells. Agonist and antagonist potency was measured using the pigment aggregation response of a clonal line of *Xenopus laevis* melanophores. The 2-methoxyisoindolo[2,1-a]indoles showed much higher binding affinities than the parent isoindoles and whereas 2-methoxyisoindolo[2,1-a]indoles were agonists in the functional assay, its cyclopropanecarbonyl derivative and parent

isoindoles were antagonists. The 2-ethoxyisoindolo[2,1-a]indoles showed reduced binding affinities compared to their methoxy analogs, while the 5-chloro derivative showed a considerable reduction in binding affinity and potency compared to acetyl 2-methoxyisoindolo[2,1-a]indole compound. The 10-methoxy-5,6-dihydroindolo[2,1-a]isoquinolines had higher binding affinities than the corresponding parent indoloisoquinolines in the human receptor subtypes, and the parent compds. were antagonists whereas the 10-methoxy derivs. were agonists in the functional assay. The N-cyclobutanecarbonyl derivs. of both the parent and 10-methoxyl series had similar binding affinities and were both antagonists with similar potencies. The 11-methoxy-6,7-5H-benzo[c]azepino[2,1-a]indoles had higher binding affinities than the corresponding parent compds. at the MT2 receptor but similar affinities at the mtl site; all of the compds. were antagonists in the functional assay. Changing 11-methoxy for 11-ethoxy decreased the binding affinity slightly, and this was more evident at the MT2 receptor. All of the derivs. investigated had either the same or a greater affinity for the human MT2 receptor compared to the mtl receptor (range 1:1-1:132). This suggests that the mtl and MT2 receptor pockets differ in their ability to accommodate alkyl groups in the indole nitrogen region of the melatonin mol. Two compds. were tested in functional assays on recombinant mtl and MT2 melatonin receptors. N-butanoyl 2-(9-methoxy-6H-isoindolo[2,1-a]indol-11-yl)ethanamine was a potent agonist with some selectivity (44-fold) for the MT2 receptor, while N-butanoyl 2-(5,6,7-trihydro-11-methoxybenzo[c]cyclohept[2,1-a]indol-13-yl)ethanamine was an MT2-preferring antagonist. Increasing the carbon chain length between N-1 of indole and the 2-Ph group from n = 1 through n = 3 leads to a fairly regular decrease in the binding affinity, but, remarkably, when n = 3, it converts the methoxy compds. from melatonin agonists to antagonists. The Xenopus melatonin receptor thus cannot accommodate an N-n-alkyl chain attached to a 2-Ph substituent with n > 2 in the required orientation to induce or stabilize the active receptor conformation.

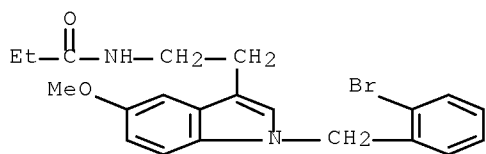
IT 263864-85-3P 263864-86-4P 263864-89-7P  
 263864-90-0P 263864-99-9P 263865-00-5P  
 263865-04-9P 263865-05-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and structure of melatonin agonists and antagonists derived from isoindoloindoles, indoloisoquinolines, and benzoazepinoindoles)

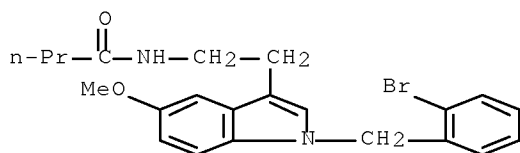
RN 263864-85-3 HCAPLUS

CN Propanamide, N-[2-[1-[(2-bromophenyl)methyl]-5-methoxy-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



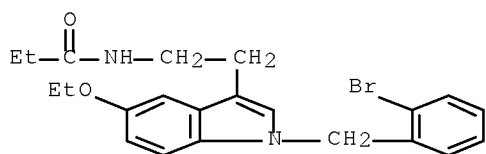
RN 263864-86-4 HCAPLUS

CN Butanamide, N-[2-[1-[(2-bromophenyl)methyl]-5-methoxy-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



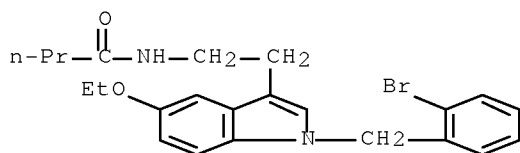
RN 263864-89-7 HCAPLUS

CN Propanamide, N-[2-[1-[(2-bromophenyl)methyl]-5-ethoxy-1H-indol-3-yl]ethyl]-  
(CA INDEX NAME)



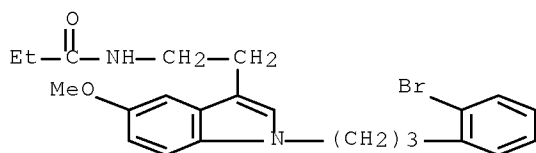
RN 263864-90-0 HCAPLUS

CN Butanamide, N-[2-[1-[(2-bromophenyl)methyl]-5-ethoxy-1H-indol-3-yl]ethyl]-  
(CA INDEX NAME)



RN 263864-99-9 HCAPLUS

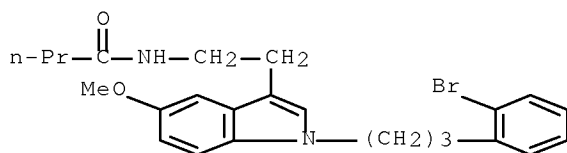
CN Propanamide, N-[2-[1-[3-(2-bromophenyl)propyl]-5-methoxy-1H-indol-3-yl]ethyl]-  
(CA INDEX NAME)



RN 263865-00-5 HCAPLUS

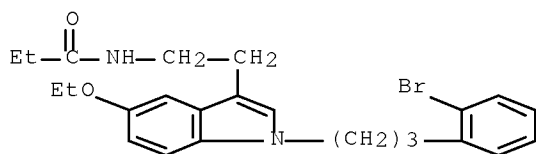
CN Butanamide, N-[2-[1-[3-(2-bromophenyl)propyl]-5-methoxy-1H-indol-3-yl]ethyl]-  
(CA INDEX NAME)





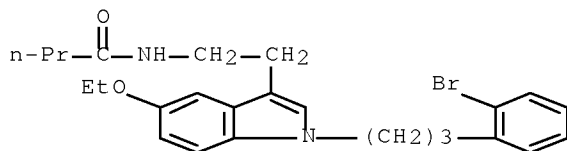
RN 263865-04-9 HCAPLUS

CN Propanamide, N-[2-[1-[3-(2-bromophenyl)propyl]-5-ethoxy-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



RN 263865-05-0 HCAPLUS

CN Butanamide, N-[2-[1-[3-(2-bromophenyl)propyl]-5-ethoxy-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



OS.CITING REF COUNT: 73 THERE ARE 73 CAPLUS RECORDS THAT CITE THIS RECORD (74 CITINGS)

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1998:454201 HCAPLUS Full-text

DOCUMENT NUMBER: 129:230562

ORIGINAL REFERENCE NO.: 129:46915a,46918a

TITLE: The chemistry of indoles. 87. Syntheses of 1-hydroxytryptamines and serotoninins having fatty acyl or (E)-3-phenylpropenoyl derivatives as a Nb-substituent, and a novel homologation on the 3-substituent of the 1-hydroxytryptamines upon treatment with diazomethane

AUTHOR(S): Somei, Masanori; Morikawa, Harunobu; Yamada, Koji; Yamada, Fumio

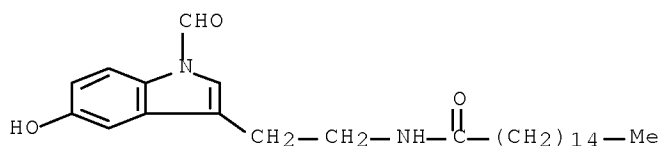
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Kanazawa University, Kanazawa, 920-0934, Japan

SOURCE: Heterocycles (1998), 48(6), 1117-1120  
CODEN: HTCYAM; ISSN: 0385-5414

PUBLISHER: Japan Institute of Heterocyclic Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 129:230562  
 AB 1-Hydroxytryptamines with (E)-3-phenyl-, (E)-3-(4-hydroxyphenyl)-, (E)-3-(4-hydroxy-3-methoxyphenyl)propenoyl, octanoyl, hexadecanoyl, and docosanoyl groups as the Nb-substituent were prepared for the first time. Preps. of serotonins from the corresponding 1-hydroxytryptamines are also reported. A new homologation on the 3-substituent of 1-hydroxytryptamines was discovered upon treatment with diazomethane in chloroform or dichloromethane.  
 IT 212707-55-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of fatty acyl or (E)-3-phenylpropenoyl derivs. of 1-hydroxytryptamines and serotonins and a novel diazomethane homologation on the 3-substituent of the 1-hydroxytryptamines)  
 RN 212707-55-6 HCAPLUS  
 CN Hexadecanamide, N-[2-(1-formyl-5-hydroxy-1H-indol-3-yl)ethyl]- (CA INDEX NAME)

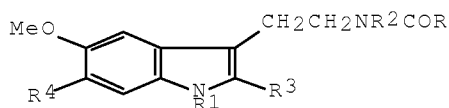


OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)  
 REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

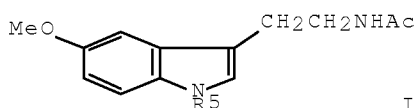
L44 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 1982:615988 HCAPLUS [Full-text](#)  
 DOCUMENT NUMBER: 97:215988  
 ORIGINAL REFERENCE NO.: 97:36249a,36252a  
 TITLE: Compound and composition for treating tumors  
 INVENTOR(S): Horst, Hans Joerg  
 PATENT ASSIGNEE(S): Fed. Rep. Ger.  
 SOURCE: Ger. Offen., 16 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3105850	A1	19820819	DE 1981-3105850	19810218
PRIORITY APPLN. INFO.:			DE 1981-3105850	19810218
OTHER SOURCE(S):			CASREACT 97:215988; MARPAT 97:215988	

GI

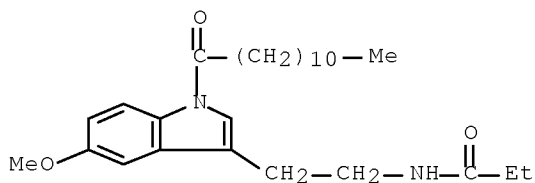


I



II

- AB Tryptamine derivs. I (R = Me, Et; R1, R2 = acyl moiety of a C9-15 carboxylic acid; R3 = H, Me; R4 = H, halo), useful in treating tumors of sex hormone-dependent organs, tissues, and(or) cells, were prepared O-Methylating 3,4-Me(O2N)C6H3OH with Me2SO4 in MeOH containing K2CO3 gave 90-95% 3,4-Me(O2N)C6H3OMe which was reduced and cyclized by catalytic hydrogenation (e.g., over Raney Ni) to give .apprx.50% 5-methoxyindole. This was cyanomethylated (successive HCHO and NaCN treatments) to give 3-(cyanomethyl)-5-methoxyindole which was reduced with BH4-, AlH3, or LiAlH4 to give 5-methoxytryptamine. This was acetylated with Ac2O to give II (R5 = H) which was acylated with Me(CH2)10COCl to give .apprx.95% diacyl derivative II [R5 = Me(CH2)10CO]. At 6 µg/mL II [R5 = Me(CH2)10CO], the prostate of a hamster gained  $29.2 \pm 7.3$  mg, whereas when II (R5 = H) was used, the weight gain was  $36.6 \pm 7.5$  mg, vs.  $59.5 \pm 11.2$  for a control.
- IT 83792-50-1F  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)
- RN 83792-50-1 HCAPLUS
- CN Propanamide, N-[2-[5-methoxy-1-(1-oxododecyl)-1H-indol-3-yl]ethyl]- (CA INDEX NAME)



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FILE 'REGISTRY' ENTERED AT 07:08:29 ON 21 OCT 2009

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L5          2378 SEA SSS FUL L3
L23         STR
L25         STR
L27         15 SEA SUB=L5 SSS FUL L23 OR L25
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L36         STR
L37         38 SEA SUB=L35 SSS FUL L36
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FILE 'HCAPLUS' ENTERED AT 08:23:13 ON 21 OCT 2009

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L39         9 SEA ABB=ON PLU=ON L27
L40         3 SEA ABB=ON PLU=ON L39 NOT L38
           D STAT QUE L40
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L41         7 SEA ABB=ON PLU=ON L29
L42         0 SEA ABB=ON PLU=ON L41 NOT (L38 OR L40)
           D STAT QUE L42
L43         9 SEA ABB=ON PLU=ON L37
L44         9 SEA ABB=ON PLU=ON L43 NOT (L38 OR L40)
           D STAT QUE L44
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